REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 1-25 will be active in the application subsequent to entry of this Amendment.

Discussion of Amended Claims

The claims have been amended in order to more particularly point out and distinctly claim that which applicants regard as their invention, to emphasize the features of method of treatment claims 10 and 21 and to address issues raised on pages 2 and 3 of the Official Action and to progress examination of this application generally.

In this Amendment the "use" claims have been revised and directed to products (*see* claims 8 and 18-20) or to include active steps (claim 7) as well as to separate a series of narrowing ranges into separate dependent claims (*see* claim 3 and its progeny new claims 22-25).

The claims also characterize the preparations/products as being ones that improve the uptake of the central cations which is discussed further in the remarks that follow.

These new and amended claims are believed to be in proper order and fully compliant with 35 USC §101 and 35 USC §112, second paragraph.

Response to Prior Art-Based Rejections

The balance of the Official Action (items 8-43) deals with a series of various prior art-based rejections directed to several different groups of claims urging that one or more of these claims are anticipated and/or lack patentable inventiveness (obvious). All of these rejections are respectfully traversed. Applicants believe that there is a fundamental misunderstanding as to the disclosures of the applied documents, in particular R2 and have taken extensive measures and investigations to confirm these concerns.

Sabin (US 5,217,959), R1 relates to the use of phosphates as active ingredients which can be used to treat MS.

The present invention relates to the uptake of essential cations whereby phosphate is the carrier to transport the essential cation.

Independent claims 1, 8, 11, 14 and 16 are above amended to include a statement of this objective to include "for improving the uptake of essential cations" to stress the difference with Sabin.

Further, Sabin teaches the treatment of MS *see* for example the summary of the invention. Sabin also teaches in the summary the use of, for example, phytic acid alone, so without counterions. Moreover Sabin teaches that all pharmaceutically counterions can be used (column 4, lines 1-46), so also for example sodium or potassium which are not essential cations may be used as well.

Hansson (US 2,834,678), R2 does not relate to phytase but rather phosphatase. This document mentions indeed phytases, but does not show that phytases were used. This document uses a phosphatase, and although a phytase is a phosphatase, not all phosphatase are phytases.

Applicants firmly believe no phytase is used. First of all the enzyme used is a phosphatase from veal bone. Because phytase has no function in bone, it is not expected that this phosphatase is a phytase. Phytases are not expected in bones because phytate is not present in bones: phytate is a plant product, so at best one may expect phytase in the gut of an animal.

To verify this point a short internet literature search was done.

A search on "mammalian phytase" resulted in:

-- Craxton, A., Caffrey, J. J., Burkhart, W., Safrany, S. T. and Shears, S. B. (1997) Molecular cloning and expression of a rat hepatic multiple inositol polyphosphate phosphatase. Biochem. J. *328*, 75-81

This concerns an liver enzyme, so it is a potential digestion related enzyme.

-- Copper, J. R. and Gowing, H. S. (1983) Mammalian small intestine phytase. *Br. J. Nutr.* 50, 673-678.

Intestine also points to a digestion-related enzyme.

A search on "animal phytase" resulted in:

-- Bing-Lan Liu, Amjad Rafiq, Yew-Min Tzeng and Abdul Rob (1998) The Induction and Characterization of Phytase and Beyond. Enzyme and Microbial Technology 22, 415-424 (copy submitted herewith in a concurrently filed IDS).

This article includes the following paragraph:

> 2.4. Phytase From Animal Tissues
>
> In comparison with the phytases of the bacteria and fungi, very little investigation of animal phytase has been undertaken. Although the specific activity of phytase has been measured from human tissue,[5] the uncertainty of phytate-splitting activity in the human small intestine and

> stomach is still remaining insofar as destruction of phytate is concerned.[71] It appears possible, however, that the activity of phytase may also be influenced by other factors (e.g., the assay method and/or in vivo or in vitro conditions). On the other hand, phytate-hydrolyzing activity has been observed in the intestinal mucosae of rat, chicken, and calves.[5] Phytase of the mammalian intestine has been suggested to be the same enzyme as alkaline phosphatase, but little is known about its subunit structure.

So again only digestion related phytatases are disclosed.

A search on: "bone enzymes phytase" resulted in:

-- LXXVIII. The occurrence of a phytin-splitting enzyme in the intestines of albino rats. Vinayak Narayan Patwardhan, Biochem J. 1937 April; 31(4): 560-564 (copy also attached with IDS).

In this article phytate is incubated with extracts of intestines of rats. In table IV results are given for phytate + intestinal and bone enzymes, bone enzymes from rabbit and rat give "nil" result with respect to phytate, whereas intestine enzymes from guinea-pig and rabbit exert action on sodium phytate.

From these articles applicants have concluded that animal bones do not contain phytase, but rather phosphatase. As stated above, applicants did not expect phytase in bones because no phytate is present in bones.

Another point in that direction is that Hansson mentions that "free inositol" is formed, which is mentioned for example in claims 1, 3, 4 and 5.

-- Wyss et al. (1999) Biochemical characterization of fungal phytases (myo-inositol hexakisphosphate phosphohydrolase): catalytic properties. Appl. Environ. Microbiol. 65:367-373 *see*:
http://aem.asm.org/cgi/content/full/65/2/367?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&fulltext=terreus&searchid=1&FIRSTINDEX=0&resourcetype=HWFIG (print attached to IDS).

Phytases catalyze hydrolysis of phytic acid, which results in the stepwise formation of IP5s, IP4s, IP3s, IP2s, and IP1s, as well as the liberation of inorganic phosphate.

The combination of phytase and acid phosphatase liberated all 6 phosphate groups. All of the fungal phytases released 5 of the 6 phosphate groups, and the end product was identified as inositol-2-monophosphate. Only in rare cases were traces of free myo-inositol detected.

In conclusion, all of the phytases investigated were able to release all 5 equatorial phosphate groups of phytic acid. Invariably, myo-inositol-2-monophosphate was identified as the end product.

So one must conclude the Hansson document teaches rather to use a phosphatase other than phytase, rather than the use of a phytase.

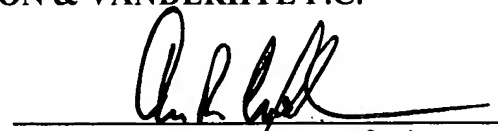
Beudeker(WO 02/05881), R3 discloses that a drink or pill containing phytase is used to deliver the phytase to humans; *see* for example page 3 of this document. The present invention relates to an "altogether" concept which comprises the phatase and phytate. Moreover according to the present invention at least part of the essential cations are bound to phytase.

In the Beudeker reference this is not necessary, for example on page 3 line 20-22, it is explained that the phytase as well as calcium is present in the milk whereas the phytic acid or phytate can be present in bread or corn flakes.

For the above reasons it is respectfully submitted that the claims of this application define inventive subject matter. Reconsideration and allowance are solicited. Should the examiner require further information, please contact the undersigned.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: 

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